

(a) a truncated glial cell line-derived neurotrophic factor (GDNF) protein product consisting of an amino acid sequence

X-(Cys<sup>41</sup>-Cys<sup>133</sup>)-Y

wherein

(Cys<sup>41</sup>-Cys<sup>133</sup>) consists of Cys<sup>41</sup> through Cys<sup>133</sup> of SEQ ID NO:2;

Y represents the carboxy terminal group of Cys<sup>133</sup>, a carboxy-terminus amino acid residue of Ile<sup>134</sup>, or a substituted amino acid residue, and

X represents a methionylated or nonmethionylated amine group of Cys<sup>41</sup> or amino-terminus amino acid residue(s) selected from the group:

G

RG

NRG

KNRG (SEQ ID NO:3)

GKNRG (SEQ ID NO:4)

RGKNRG (SEQ ID NO:5)

ORGKNRG (SEQ ID NO:6)

GORGKNRG (SEQ ID NO:7)

RGORGKNRG (SEQ ID NO:8)

RRGORGKNRG (SEQ ID NO:9)

G RRGORGKNRG (SEQ ID NO:10)

KG RRGORGKNRG (SEQ ID NO:11)

GKG RRGORGKNRG (SEQ ID NO:12)

RGKG RRGORGKNRG (SEQ ID NO:13)

SRGKG RRGORGKNRG (SEQ ID NO:14)

NSRGKG RRGORGKNRG (SEQ ID NO:15)

ENSRGKG RRGORGKNRG (SEQ ID NO:16)

PENSRGKG RRGORGKNRG (SEQ ID NO:17)

NPENSRGKG RRGORGKNRG (SEQ ID NO:18)

ANPENSRGKG RRGORGKNRG (SEQ ID NO:19)

A ANPENSRGKG RRGORGKNRG (SEQ ID NO:20)

AA ANPENSRGKG RRGORGKNRG (SEQ ID NO:21)

AAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:22)

OAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:23)

ROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:24)

NROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:25)

RNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:26)

ERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:27)

RERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:28)

RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:29)

P RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:30)

LP RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:31)

VLP RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:32)

AVLP RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:33)

MAVLP RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:34)

OMAVLP RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:35)

KOMAVLP RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:36)

DKOMAVLP RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:37) and

PDKOMAVLP RRERNROAAA ANPENSRGKG RRGORGKNRG (SEQ ID NO:38)

or a substitution or deletion variant of X, wherein said variant is in excess of 70% identical to an amino acid sequence of X as set forth above when four gaps in a length of 100 amino acids may be introduced to assist in that alignment, and

(b) a pharmaceutically acceptable vehicle.

Please add the following claims:

-- 45. (Newly added) A method for affecting the survival or function of neurons comprising administering a pharmaceutical composition comprising:

(a) a truncated glial cell line-derived neurotrophic factor (GDNF) protein product consisting of an amino acid sequence

X-(Cys<sup>41</sup>-Cys<sup>133</sup>)-Y

wherein

(Cys<sup>41</sup>-Cys<sup>133</sup>) consists of Cys<sup>41</sup> through Cys<sup>133</sup> of SEQ ID NO:2;

Y represents the carboxy terminal group of Cys<sup>133</sup>, a carboxy-terminus amino acid residue of Ile<sup>134</sup>, or a substituted amino acid residue, and

X represents a methionylated or nonmethionylated amine group of Cys<sup>41</sup> or amino-terminus amino acid residue(s) selected from the group:

G

RG

NRG

KNRG (SEQ ID NO:3)

GKNRG (SEQ ID NO:4)

RGKNRG (SEQ ID NO:5)

QRGKNRG (SEQ ID NO:6)

GQRGKNRG (SEQ ID NO:7)

RGQRGKNRG (SEQ ID NO:8)

RRGQRGKNRG (SEQ ID NO:9)

G RRGQRGKNRG (SEQ ID NO:10)

KG RRGQRGKNRG (SEQ ID NO:11)

QKG RRGQRGKNRG (SEQ ID NO:12)

RGKG RRGQRGKNRG (SEQ ID NO:13)

SRGKG RRGQRGKNRG (SEQ ID NO:14)

NSRGKG RRGQRGKNRG (SEQ ID NO:15)

ENSRGKG RRGQRGKNRG (SEQ ID NO:16)

PENSERGKG RRGQRGKNRG (SEQ ID NO:17)

NPENSERGKG RRGQRGKNRG (SEQ ID NO:18)

ANPENSERGKG RRGQRGKNRG (SEQ ID NO:19)

A ANPENSERGKG RRGQRGKNRG (SEQ ID NO:20)

AA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:21)

AAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:22)

QAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:23)

RQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:24)

NRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:25)

RNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:26)

ERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:27)

RERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:28)

RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:29)

P RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:30)

LP RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:31)

VLP RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:32)

AVLP RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:33)

MAVLP RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:34)

QMAVLP RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:35)

KQMAVLP RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:36)

DKQMAVLP RRERNRQAAA ANPENSERGKG RRGQRGKNRG (SEQ ID NO:37) and

PDKQMAVL P RRERNRQAAA ANPENS RGKG RRGQRGKNRG (SEQ ID NO:38); and

(b) a pharmaceutically acceptable vehicle.

46. A method according to Claim 30 or 45, wherein X is selected from the group consisting of SEQ ID NO: 3, 7, 8, 14, 17 and 18

47. A method according to Claim 30 or 45, wherein X is G, RG or NRG.

48. A method according to Claim 30 or 45, wherein said GDNF protein product has the amino acid sequence of SEQ ID NO:42.

49. A method according to Claim 30 or 45, wherein said GDNF protein product has the amino acid sequence of SEQ ID NO:44.

50. A method according to Claim 30 or 45, wherein said GDNF protein product has the amino acid sequence of SEQ ID NO:46. --

Respectfully submitted,

*Daniel R. Curry*

Daniel R. Curry  
Attorney for Applicant  
Registration No.: 32,727  
Phone: (805) 447-8102  
Date: October 13, 2000

Please send all future correspondence to:

U.S. Patent Operations/ DRC  
Dept. 4300, M/S 27-4-A  
AMGEN INC.  
One Amgen Center Drive  
Thousand Oaks, California 91320-1799